

## Newborn Screening Quality Assurance Program

- **Services provided:**
  - Filter paper evaluation
  - Reference materials
  - Quality control materials
  - Proficiency testing
  - Training, consultations, network resources
- **Partners**
  - Association of Public Health Laboratories
  - 73 domestic screening laboratories
  - Laboratories in 54 countries
  - 400 plus screening laboratories worldwide

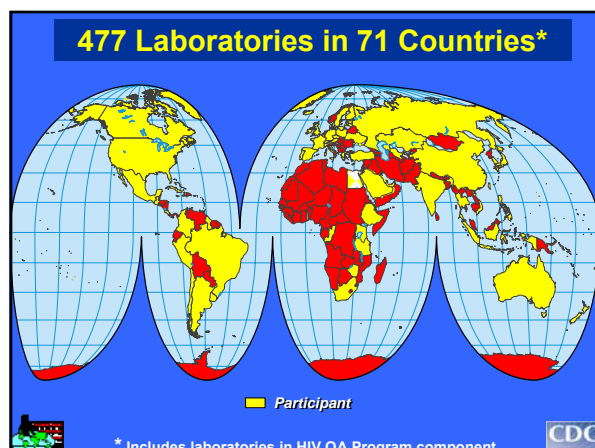
<http://www.cdc.gov/labstandards/nsqap.htm>

**CDC**

## History of the Newborn Screening Quality Assurance Program

- 1978 - Congenital Hypothyroidism
- 1984 - PKU, MSUD, Homocystinuria
- 1986 - Galactosemia
- 1987 - HIV Seroprevalence Survey
- 1988 - Congenital Adrenal Hyperplasia
- 1991 - Sickle Cell Disorders
- 1997 - Biotinidase
- 2001 - Fatty Acid and Organic Acid Disorders
- 2002 - Cystic Fibrosis, Diabetes
- 2005 - Toxoplasmosis
- **2006 - 35 plus disorders and growing**

**CDC**

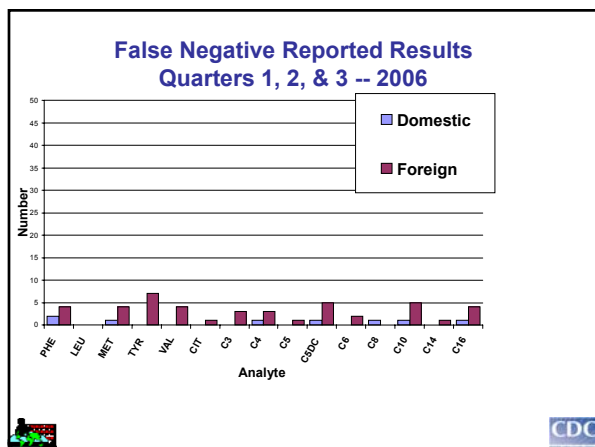
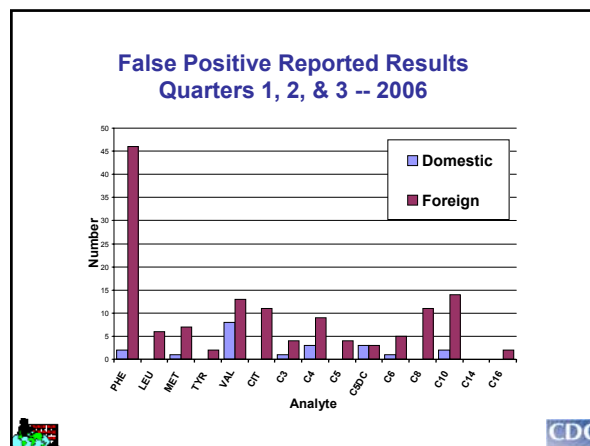
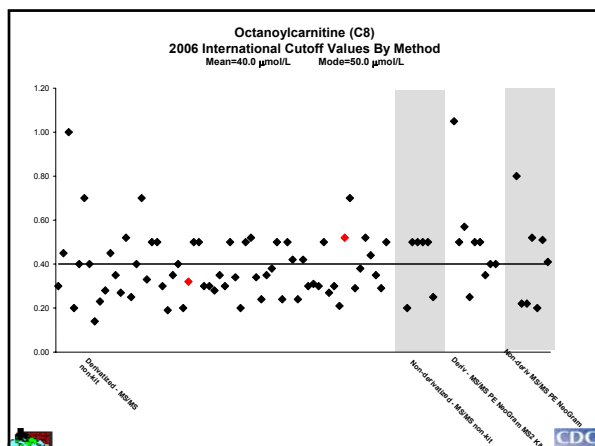


## Analytes/Biomarkers included in NSQAP

• Biotinidase	• Hexanoylcarnitine (C6)
• Thyroxine	• Octanoylcarnitine (C8)
• Thyroid-stimulating hormone	• A985G MCAD mutation
• 17 $\alpha$ -hydroxyprogesterone	• Decanoylcarnitine (C10)
• Total galactose	• Myristoylcarnitine (C14)
• Uridyltransferase (GALT)	• Palmitoylcarnitine (C16)
• Citrulline	• Immunoreactive trypsinogen
• Phenylalanine	• $\Delta$ 508 mutations
• Leucine	• Hemoglobinopathies and SS, SC, SD, SE mutations
• Valine	• Diabetes Type 1 risk mutations
• Methionine	• Toxoplasmosis: IgG, IgM
• Tyrosine	• HIV type 1 antibodies
• Propionylcarnitine (C3)	• Creatine kinase (DMD)
• Isobutyrylcarnitine (C4)	• Androstenedione/cortisol
• Isovalerylcarnitine (C5)	
• Glutarylarnitine (C5DC)	

**CDC**





Newborn Screening  
Quality Assurance Program

New and Pilot Initiatives

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Second Tier Testing: Congenital Adrenal Hyperplasia by LC/MS/MS

- LC/MS/MS developed and applied for improved specificity for detecting CAH
- Measurements made on presumptive positives identified by immunoassay
- Method measures three hormones: 17- $\alpha$  hydroxyprogesterone (17-OHP), androstenedione (4-AD) and cortisol
- Elevated 17-OHP and 4-AD, and depressed cortisol are a positive indication of CAH
- The ratio of  $\frac{[17-OHP] + [4-AD]}{[Cortisol]}$  is used as a cutoff

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## QA/QC/PT Materials for Second Tier CAH Test (LC/MS/MS)

- Used hormone free serum
- Spiked with all 3 hormones (ratios) to control EIA and LC/MS/MS results independently
- Androstenedione and cortisol levels do not interfere with 17-OHP testing by EIA
- Designed DBS specimens to mimic True Negative, True Positive, and False Positive.
- Quarterly DBS distributed to 4 Laboratories
- DBS QC/PT's available for other laboratories



## Lab Challenge Samples

Sample	Final 17-OHP (nM/L)	Final 4-AD (nM/L)	Final Cortisol (nM/L)	Expected LC-MS/MS Ratio (0.58 x [17-OHP] + 1.03 x [4-AD]) (0.19 x [Cortisol])
True Negative	75.7	41.9	344.9	1.33
True Positive	227.0	122.2	165.5	8.19
False Positive	227.0	0.0	344.9	2.01
Cutoff Sample	151.3	87.3	264.9	3.53
Base Sample	0.0	0.0	0.0	N/A

True Positive and False Positive have the same 17-OHP concentration, but different 4-AD and Cortisol levels.

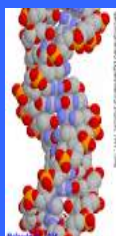
Cutoff specimen has 17-OHP value near EIA cutoff and expected ratio cutoff.

All specimens were made with hormone-free base serum.



## Phenotype/Genotype Blood-spot Quality Assurance Materials

- Cystic fibrosis
- Hemoglobinopathies
- Medium-chain acylcarnitine dehydrogenase deficiency\*
- Galactosemia
- Biotinidase deficiency
- Diabetes type 1



\* Under development



## New Disorders on the Horizon for NSQAP



- Diabetes Risk Screening (Pilot Project ongoing)
- ▶ Severe Combined Immunodeficiency (SCID)
- Lysosomal Storage Disorders (Meeting 12/ 2005)
- ▶ Duchenne muscular dystrophy (Fall 2005 - 6 labs)



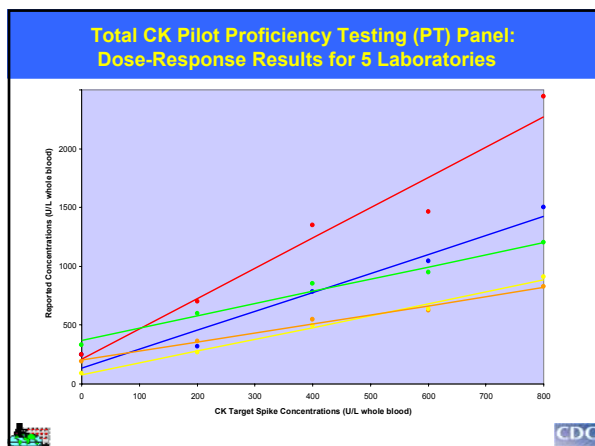
## DEVELOPING A QUALITY ASSURANCE PROGRAM FOR DUCHENNE MUSCULAR DYSTROPHY SCREENING



## NSQAP provides to the DMD laboratory Participants:

- Quality Control DBS materials
- Proficiency Testing DBS materials
- Dose-response (Calibrators) materials
- Technical consultations and analytic services
- Quarterly and annual reports





### FUTURE PLANS FOR DMD

- Improve comparability of lab measurements
- Distribute total CK - QC and PT materials
- Prepare and distribute PT reports
- Prepare isoenzyme-specific CK materials
- Obtain blood samples from confirmed DMD patients for use in a DNA-based PT panel – phenotype/genotype challenges

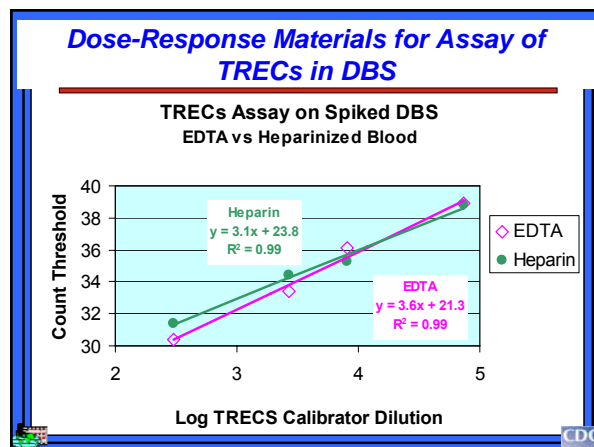
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### Severe Combined Immunodeficiency Screening: Real-time PCR Assay for TREC in Dried Blood Spots

- Multiplexed Assay with Single Reaction Mixture
- Highly Sensitive - Similar to HIV Viral Load Assay

**\*\* Transfected HeLa Cells Developed for Production of TREC Calibrators, Controls and PT \*\***

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### Newborn Screening Quality Assurance

Request information about the Newborn Screening Quality Assurance Program

User Login

Public Reports (Nov 9)

**"Expanding to Serve your Needs Thank You!"**

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